

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Meng YANG et al.

Application No.: 10/714,068

Filed: November 14, 2003

For: WHOLE-BODY OPTICAL IMAGING OF
GENE EXPRESSION AND USES THEREOF

Confirmation No.: 2630

Art Unit: 1636

Examiner: Celine X. Qian, Ph. D.

DECLARATION OF ROBERT M. HOFFMAN

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, ROBERT M. HOFFMAN, declare as follows:

1. I am a Professor in the Department of Surgery at the University of California San Diego Medical Center and am Chairman of the Board and Chief Executive Officer of AntiCancer, Inc., the assignee herein. I have been engaged in diagnostics and laboratory models employing fluorescent protein expression for at least the past 10 years. I obtained my Ph.D. in biology from Harvard University in 1971 and have been practicing in the field of cancer research since that time. I have held academic positions at Harvard Medical School and at the Weizmann Institute and have published about 400 articles on subjects related to cancer and metastasis. I am on the editorial

boards of *AntiCancer Research*, of *Clinical Cancer Research* and of *In Vitro Cellular and Developmental Biology*. A copy of my *curriculum vitae* is attached as Exhibit A.

2. I have reviewed the patent application captioned above and the Office action mailed 25 June 2007, in particular the basis for rejection of claims 39 and 40 under 35 U.S.C. § 112, first paragraph. The Office asserts that these claims lack enablement because observing the presence, absence or intensity of fluorescence of a protein encoded by a nucleotide sequence operably linked to a promoter would not reliably reflect the interaction of a test compound with the promoter. The Office asserts this is in view of complicating factors such as “drug interaction and metabolism.” While it is not entirely clear what is meant by “drug interaction and metabolism” in this context, it is perhaps explained by an earlier statement referred to, that the “intensity of the fluorophore may be the result of interaction with another gene product.”

3. From my experience in dealing with animal models involving fluorescent proteins as indicators, I believe that the occurrence of such interaction would be extremely rare, if existent at all, since I am aware of no mechanism whereby the fluorescence of such proteins is interfered with by other metabolites. Fluorescent proteins have been used as reporters for many years. Nevertheless, should this be of concern, the practitioner could readily control for such an occurrence in a very straightforward manner as follows:

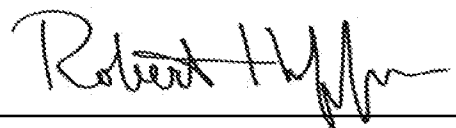
4. A straightforward control would be to place the fluorescent protein-encoding sequence under control of a housekeeping promoter whose ability to control expression is known not to be affected by the test compound used. If indeed the effect of the test compound is only on the promoter being targeted, the level of fluorescence of the control would be identical in both the presence and absence of the test compound. If, for some reason, there is an impact of the compound

on some other metabolite which somehow interferes with the fluorescence of the fluorescent protein or intensifies it, this will be evident in the control.

5. In view of the absence of any known instances in which the fluorescence activity of a reporter fluorescent protein is altered by an additional metabolite, and in view of the ready availability of a control to verify that this is the case, I believe that the presence, absence or level of fluorescence of the reporter protein is a reliable index of the activity of the promoter that has been operatively linked to the encoding sequence for said protein and thus of the effect of a test compound on that promoter.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at San Diego, on 28 August 2007.

A handwritten signature in black ink, appearing to read "Robert Hoffman", written over a horizontal line.

ROBERT M. HOFFMAN

Application No.: 10/714,068

Docket No.: 312762002710

enclosures:

curriculum vitae

CURRICULUM VITAE

ROBERT M. HOFFMAN

September 2007

CURRICULUM VITAE

ROBERT M. HOFFMAN

OFFICES: AntiCancer, Inc.
7917 Ostrow Street
San Diego, California 92111
TEL: (858) 654-2555
FAX: (858) 268-4175

Department of Surgery
University of California, San Diego
Medical Center
200 West Arbor Drive
San Diego, California 92103-8402
TEL: (619) 543-6890
FAX: (619) 543-3763

BIRTH DATE: June 19, 1944
Greenwich, Connecticut

EDUCATION: Ph.D. (Biology) 1971
Harvard University
Cambridge, Massachusetts

B.A. (Biology) 1965
State University of New York
Buffalo, New York

PRESENT POSITIONS: President, Chairman of Board and CEO 1984-present
AntiCancer, Inc.
San Diego, California

Professor 1995-present
Department of Surgery
University of California, San Diego
Medical Center
200 West Arbor Drive
San Diego, California 92103-8220

MAJOR RESEARCH ACCOMPLISHMENTS:

1. Discovery of DNA hypomethylation in human cancer cells (1982).
2. Discovery of the first hypomethylated oncogene in cancer cells (1984).
3. Originator of concept of methylation-based cancer epigenetics (1984).
4. Pioneer of highly-selective anti-methionine cancer therapy based on methioninase (1993).
5. Pioneer of DNA-containing liposomes (1978) – the enabling technology for non-viral *in vivo* gene therapy.
6. Pioneer of "patient-like" animal models for cancer – "MetaMouse[®]" (1988).
7. Pioneer of an *in vivo*-like 3-D model of human tumor culture and drug-sensitivity testing – "HDRA[®]", (1986).
8. Pioneer of an *in vitro* hair growth model from human and animal skin (1991).
9. Pioneer of a hair follicle-specific drug and gene targeting system (1992).
10. Discovery of the governing step of metastasis (1995).
11. Pioneer of use of green fluorescent protein (GFP) *in vivo* (1997).
12. Pioneer of whole-body fluorescence imaging for cancer metastasis, gene expression, and bacterial infection (2000).
13. Pioneer of enzyme-activated prodrug gene therapy with the methioninase gene and selenomethionine (2001).
14. Pioneer of the first single-enzyme assay for homocysteine (1998).
15. Pioneer of the first homogeneous non-radioactive assay for vitamin B₆ (2002).
16. Discovery of the pluripotency of hair-follicle stem cells to form neurons and other non-hair follicle cells (2003).
17. Pioneer of bacterial monotherapy of cancer (2005).

POSTDOCTORAL TRAINING:

Department of Biology Harvard University With the late Professor John R. Raper	1971-1973
Massachusetts General Hospital Harvard Medical School With Dr. Richard W. Erbe and Professor John W. Littlefield	1973-1975
USA-USSR National Academy of Sciences Exchange Fellow The Shemyakin Institute of Bioorganic Chemistry Academy of Sciences, Moscow, USSR With Professor L.D. Bergelson	1976-1977
Weizmann Institute of Science Rehovot, Israel With Dr. Carol Prives	1978

PREVIOUS ACADEMIC POSITIONS:

Instructor of Pediatrics Harvard Medical School Massachusetts General Hospital	1975-1979
Assistant Professor, Department of Pediatrics University of California, San Diego School of Medicine	1979-1983

Associate Professor, Department of Pediatrics University of California, San Diego School of Medicine	1983-1990
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Professor, Department of Pediatrics University of California, San Diego School of Medicine	1990-1995
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PROFESSIONAL SOCIETIES:

1. Society for *In Vitro* Biology
2. American Association of Cancer Research
3. American Society for Clinical Oncology
4. Society of Surgical Oncology
5. American Society for Cell Biology
6. Metastasis Research Society
7. Japanese Cancer Association
8. Japanese Society of Clinical Oncology (First American Member)
9. Japanese Metastasis Research Society (First American Member)
10. Japanese Society of Human Cell
11. Preclinical Therapeutic Model Group of the European Organization for Research and Treatment of Cancer
12. Chinese Society for Clinical Oncology (First American Member)
13. International Society for Stem Cell Research

BOARDS:

Ad-Hoc Reviewer National Cancer Institute	1986-present
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EDITORIAL BOARDS:

<i>Anticancer Research</i>	1985-present
<i>In Vitro Cellular and Developmental Biology</i>	1987-present
Associate Editor, <i>Clinical Cancer Research</i>	2000-Present

TEACHING AT THE UNIVERSITY OF CALIFORNIA, SAN DIEGO:

Biology 112:	"Cell and Molecular Biology" Spring and Fall With Professor Gordon Sato	1980
Pediatrics 233:	"Genes and Cancer" Winter	1982-1994
Pediatrics 235:	"New Biological Approaches to Cancer Prevention and Treatment" Spring	1983-1994
Pediatrics 237:	"Biochemical Genetics of Aging" Fall	1984-1994

UNIVERSITY COMMITTEES:

Admissions Committee University of California, San Diego School of Medicine	1983-1985
Electives Committee University of California, San Diego School of Medicine	1989-1990

HONORS AND AWARDS:

Honorary Professor Harbin Medical University Harbin, China	1994
Honorary Member Keio University Department of Surgery Tokyo, Japan	1991
A.N. Belozersky Medal Moscow State University	1990
Research Career Development Award National Cancer Institute	1982-1987
Fellow of the Leukemia Society of America	1979-1981
Fellow of the Medical Foundation of Boston	1976-1977
United States National Academy of Sciences Exchange Fellowship Shemyakin Institute of Bioorganic Chemistry Moscow, USSR.	1976-1977
Postdoctoral Fellowship Awardee National Institutes of Health	1974, 1976, 1978
National Institutes of Health Postdoctoral Training Grant Fellow Harvard Medical School	1973-1974
Postdoctoral Research Fellow Harvard University	1971-1973
National Institutes of Health Training Grant Predoctoral Fellowship Harvard University	1966-1971
Phi Beta Kappa State University of New York Buffalo, New York	1964

PLENARY LECTURES:

- International Symposium on "The biochemistry
of S-adenosylmethionine as a basis of drug design" 1985
Bergen, Norway
Lecture entitled "Cancer, methionine and transmethylation. "
- Federation of American Societies for 1986
Experimental Biology Summer Research Conference entitled
"Folic acid, B-12, and one-carbon metabolism"
Saxtons River, Vermont
Lecture entitled "Altered methionine metabolism and transmethylation
in human cancer cells."
- Gordon Research Conference on Cancer 1987
New London, New Hampshire
Lecture entitled "Methionine, transmethylation and cancer."
- Invited lecturer, Tissue Culture Association Conference 1988
Las Vegas, Nevada
Lecture entitled "Partitioning of methyl groups in cancer and normal cell types."
- Federation of American Societies for 1989
Experimental Biology Summer Research Conference
Copper Mountain, Colorado
Lecture entitled "Cancer, methionine metabolism and transmethylation."
- Invited Lecturer, Dae Han Biochemical Society 1990
Seoul, Korea
Lecture entitled "Altered methionine metabolism, unbalanced
global cellular transmethylation and cancer."
- Invited Lecturer, Korean Association of Molecular Biology 1990
Pusan, Korea
Lecture entitled "Rational evaluation and design of cancer drugs. "
- Third International Conference of Anticancer Research 1990
Marathon, Greece
Lecture entitled "The development of clinically relevant *in vitro* and *in vivo*
preclinical models: Three-dimensional gel-supported *in vitro* histoculture and
orthotopic implantation and metastasis of human tumors in nude mice. "
- Invited Lecturer, Regina Elena Cancer Center 1991
Rome, Italy
Lecture entitled "Patient-like *in vitro* and *in vivo* pre-clinical models of human cancer."
- Gordon Research Conference on Cancer Chemotherapy 1992
New London, New Hampshire
Lecture entitled "Orthotopic-transplantation animal models for the identification
of new anticancer drugs. "

Fourth International Congress of the Metastasis Research Society Paris, France Lecture entitled "The nude mouse comes to the cancer clinic: Metastatic models of the major cancer types constructed by orthotopic transplantation of histologically-intact patient specimens."	1992
First Congress of the International Society for Experimental Microsurgery Rome, Italy Lecture entitled "Microsurgery, orthotopic human tumor transplantation and the nude mouse: Patient-like metastatic models of human cancer. "	1992
Keystone Symposium on Discovery and Development of Therapeutic Compounds Snowmass, Colorado Session Chairman, Lecture entitled "Orthotopic models for treatment evaluation <i>in vivo</i> using histologically-intact cancer patient specimens."	1993
FASEB Summer Conference Copper Mountain, Colorado Lecture entitled "MetaMouse [®] : the nude mouse comes to the cancer clinic via orthotopic transplantation of architecturally-intact patient tumors. "	1993
Hellenic Society for Breast Cancer Research, First International Congress Corfu, Greece Lecture entitled "Patient-like cancer models and therapeutics specific for cancer- an approach to the next generation of treatment"	1993
FASEB Summer Conference Copper Mountain, Colorado Lecture entitled "Tissue architecture and metastases"	1994
Japan Society of Human Cell Meeting Toyoma City, Japan Lecture entitled " <i>In vitro</i> drug response assays are clinically useful in cancer"	1995
Hellenic Society For Breast Cancer Research, Second International Congress Kos Island, Greece Lecture entitled "Methioninase (AC9301): A selective antitumor agent with a new mechanism of action."	1995
6th International Congress on Anticancer Treatments Paris, France Lecture entitled "Pilot phase I clinical trial of methioninase: serum depletion of methionine without acute toxicity."	1996
6th International Congress on Anticancer Treatments Paris, France Lecture entitled "The gelatinase-A Inhibitor CT1746 arrests human colon tumor growth and spread and increases survival in a patient like orthotopic model in nude mice."	1996

IBC USA Alopecia Conference San Diego, California Lecture entitled "The feasibility of targeted selective gene therapy of the hair follicle."	1996
Shanghai International Symposium on Liver Cancer & Hepatitis Shanghai, China Lecture entitled "Liver colonization capability governs metastatic potential"	1996
Cambridge Healthtech Institute's Engineered Animal Models Baltimore, Maryland Lecture entitled "MetaMouse [®] Models of Cancer: Clinically Relevant Orthotopic Models of Cancer Growth and Metastasis"	1996
Third International Conference of the Asian Clinical Oncology Society (ACOS) Kunming, China Lecture entitled "Taking chemotherapy from random to rational with the histoculture drug response assay"	1996
The International Congress on Human Cell and Cell Culture Tokyo, Japan Lecture entitled "Nutritional regulation of cancer growth by use of methioninase: possible apoptotic cell kill mechanism"	1996
The Sixth International Congress of the Metastasis Research Society Gent, Belgium Lecture entitled "Surgical Orthotopic Implantation (SOI): A new approach to develop clinically-relevant models of human metastatic cancer in immunodeficient rodents"	1996
IBC's Alopecia Conference Washington, D.C. Lecture entitled "Hair Follicle Targeting of Large and Small Molecules with Topical Liposomes"	1996
First Panhellenic Congress of Tumors Markers with International Participation Athens, Greece Lecture entitled "Methionine dependence as a Possible Universal Therapeutic Tumor Marker"	1996
Seventh International Congress on Anticancer Treatment (SOMPS) Paris, France Lecture entitled "R-Methioninase as a potential universal apoptotic antitumor agent"	1997
Seventh International Congress on Anticancer Treatment (SOMPS) Paris, France Lecture entitled "Acquisition of broad range multidrug resistance in recurrent breast cancer"	1997

IBC's Drug Discovery Approaches to Cosmeceuticals Conference East Rutherford, NJ Lecture entitled "Hair producing histoculture skin for the discovery of a new generation of hair follicle targeted cosmeceuticals and therapeutics"	1997
30th Annual Meeting of the Japanese Research Society for Appropriate Cancer Chemotherapy Tokyo, Japan Lecture entitled "Histoculture Drug Response Assay"	1997
IBC's Delivery Technologies for Cosmetic Ingredients Conference Philadelphia, PA Lecture entitled "Cosmetic and therapeutic molecules targeted to hair follicles by topical liposomal application"	1997
6th Hellenic Congress on Senology and the 3rd International Congress of the Hellenic Society for Breast Cancer Research Alexandroupolis, Greece Lecture entitled "Cachexia in breast cancer and elevated amino-acid requirements of tumors: Selective biological targets for therapy"	1997
FASEB Summer Research Conference on Biological Methylation Saxtons River, Vermont Lecture entitled "Alterations in methionine dependence and transmethylation in cancer: methioninase for therapy"	1997
3 rd International Symposium on Polymer Therapeutics London, England Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase for cancer therapy"	1998
8 th International Congress on Anti-Cancer Treatment Paris, France Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase for cancer therapy"	1998
Gordon Research Conference on Lasers in Medicine and Biology Meriden, New Hampshire Lecture entitled "Green fluorescent protein: A new light to study metastasis and angiogenesis"	1998
25 th Balken Medical Week Conference Ioannina, Greece Lecture entitled "Methioninase: A new selective cancer therapy"	1998
7 th Annual Meeting of the Japanese Association for Metastasis Research Sapporo, Japan Lecture entitled "Green fluorescent protein: A new light to study the role of angiogenesis in metastasis"	1998

SPIE's International Symposium on Biomedical Optics San Jose, CA Lecture entitled "Green fluorescent protein: A new light to visualize metastasis and angiogenesis in cancer"	1999
2 nd International Symposium on GFP – The Green Fluorescent Protein San Diego, CA Lecture entitled "Fluorescent optical tumor imaging (FOTI) of human cancers in live nude mice"	1999
4 th International Conference of the Asian Clinical Oncology Society (ACOS) Bali, Indonesia Lecture entitled "Individualizing cancer chemotherapy by tumor histoculture"	1999
58 th Annual Meeting of the Japanese Cancer Association Hiroshima, Japan Lecture entitled "Orthotopic transplant mouse models with green fluorescent protein-expressing cancer cells to visualize micrometastasis and angiogenesis"	1999
SPIE's International Symposium on Biomedical Optics San Jose, CA Lecture entitled "External optical imaging of green fluorescent protein-expressing metastatic tumors"	2000
VIII International Congress of the Metastasis Research Society London, UK Lecture entitled "GFP tumor, metastases, and angiogenesis whole-body imaging"	2000
9 th Shizuoka Drug Delivery Conference Shizuoka, Japan Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase for cancer therapy"	2000
World Congress on In Vitro Biology San Diego, California Lecture entitled "Individualized cancer chemotherapy by tumor histoculture"	2000
13 th International Congress on Photobiology San Francisco, California Lecture entitled " <i>In vivo</i> high-throughput drug screen with whole-body imaging GFP tumor models"	2000
11 th International Symposium for Bioluminescence and Chemiluminescence Monterey, California Lecture entitled "Whole-body optical imaging of green fluorescent protein-expressing tumors"	2000
3 rd International Symposium on Minimal Residual Cancer Hamburg, Germany Lecture entitled "Mouse Models: Whole-body and intra-vital fluorescence imaging of minimal residual disease, tumor growth and progression"	2001

54 th Annual Cancer Symposium of the Society of Surgical Oncology Washington, DC Lecture entitled “Visualizing gene expression by whole-body fluorescence imaging”	2001
Asan Medical Center, Dept. of General Surgery and Div. Of Hematology/Oncol. Seoul, Korea Special Lecture entitled “The clinical significance of Histoculture Drug Response Assay (HDRA) in solid tumors”	2001
92 nd Annual American Association for Cancer Research Annual Meeting Educational Session 7 – Approaches in Drug Development and Toxicology New Orleans, Louisiana Lecture entitled “Whole-body fluorescence imaging of GFP of tumor growth, Metastasis, angiogenesis and gene expression”	2001
NCI Mouse Models of Human Cancers Consortium Preclinical Trials Meeting Bethesda, MD Lecture entitled “ <i>In vivo</i> imaging”	2001
NIH Mouse Models of Mammary Cancer Consortium Meeting Bethesda, MD Lecture entitled “Whole-body fluorescence imaging with GFP of tumor growth, metastasis, angiogenesis and gene expression”	2001
62 nd Annual Meeting of the Society of Investigative Dermatology Washington, DC Oral Presentation “Gene therapy of growing hair shafts”	2001
NCI Mouse Models of Human Cancers Consortium Lung Cancer Workshop Boston, MA Lecture entitled “GFP imaging of lung tumors in nude mice”	2001
29 th Annual Meeting of the American Society for Photobiology Chicago, IL Lecture entitled “Real-time whole-body fluorescence imaging of bacterial infection”	2001
NCI Preclinical Angiogenesis Imaging Models Working Group Meeting Washington, DC Lecture entitled “GFP imaging of angiogenesis in mice”	2001
IIR’s 3 rd Annual Conference on Angiogenesis: Innovative Science and New Applications Boston, MA Lecture entitled” Whole-body and intravital optical imaging of angiogenesis in orthotopically implanted tumors”	2001
2 nd Annual Molecular Imaging Workshop East Lansing, MI Lecture entitled “Whole-body fluorescence imaging with GFP of tumor growth, metastasis, angiogenesis and gene expression”	2001

15 th Annual BACT Symposium Nagoya, Japan Lecture entitled “ <i>In vitro</i> chemosensitivity as a predictor of outcome in patients with head and neck cancer”	2001
University of Texas NSF IGERT Program Seminar Austin, TX Lecture entitled “Whole-body imaging of tumors, metastasis, micrometastasis, angiogenesis and gene expression”	2001
Massachusetts General Hospital, Wellman Laboratories of Photomedicine Lecture Series Boston, MA Lecture entitled “Optical imaging with GFP”	2002
Sidney Kimmel Cancer Center Seminar Series San Diego, CA Lecture entitled “Optical imaging with GFP”	2002
SPIE’s BIOS 2002 Symposium – Conference on Functional Imaging and Optical Manipulation of Living Cells and Tissues San Jose, CA Lecture entitled “Fluorescence imaging of angiogenesis in green fluorescent protein-transduced tumors”	2002
European School of Haematology’s Animal Models of Human Disease: Modeling Human Cancers in the Mouse: A Practical Issue Paris, France Lecture entitled “Whole-body fluorescence imaging of tumor growth, micrometastasis, metastasis, angiogenesis and gene expression”	2002
Showa University, Northern Yokohama Hospital Yokohama, Japan Lecture entitled “Green fluorescent protein imaging of cancer”	2002
UCLA Crump/General Electric/LSI Molecular Imaging Seminar Series Los Angeles, CA Lecture entitled “Optical imaging with GFP”	2002
93 rd Annual Meeting of the American Association for Cancer Research San Francisco, CA Lecture entitled “Direct external imaging of nascent cancer, tumor progression, angiogenesis, and metastasis on internal organs in the fluorescent orthotopic model”	2002
University of Texas of M.D. Anderson Cancer Center – Dept. of Cancer Biology’s Cancer Metastasis Research Program Seminar Series Houston, TX Lecture entitled “Optical imaging with GFP”	2002

Netherlands Cancer Institute Symposium: In the Footsteps of Antoni Van Leeuwenhoek Amsterdam, Netherlands Lecture entitled “Non-invasive visualization of fluorescent tumors in intact animals”	2002
6 th Joint Meeting of the Japan Society of Histochemistry and Cytochemistry and the Histochemical Society Seattle, WA Lecture entitled “Non-invasive visualization of fluorescent tumors in intact animals”	2002
9 th Annual Meeting of the European Hair Research Society Brussels, Belgium Lecture entitled “Selective hair follicle targeting”	2002
6 th Congress of the International Society for Experimental Microsurgery San Diego, CA Lecture entitled “Direct external imaging of nascent cancer, tumor progression, angiogenesis, and metastasis on internal organs in the fluorescent orthotopic model”	2002
1 st Annual Meeting of the Society of Molecular Imaging Boston, MA Lecture entitled “Multi-color imaging with fluorescent proteins”	2002
9 th International Congress of the Metastasis Research Society Chicago, IL Lecture entitled “Dual-color imaging of tumors and metastasis in mice”	2002
2 nd Petersberg Euroconference Petersberg, Germany Lecture entitled “ <i>In vivo</i> fluorescence resonance energy transfer (FRET) measurement”	2002
Jichi Medical School Jichi, Japan Lecture entitled “Green fluorescent protein imaging of tumor cells <i>in vivo</i> ”	2002
Dana-Farber/Harvard Cancer Center Cancer Cell Biology Program’s Minisymposium on Molecular Imaging Boston, MA Lecture entitled “Dual-color <i>in vivo</i> imaging of cancer”	2002
The Hebrew University of Jerusalem Jerusalem, Israel Lecture entitled “A hair-brain connection: Nestin expressing hair follicle stem cells”	2003
The Hebrew University of Jerusalem Jerusalem, Israel Lecture entitled “Whole-body optical imaging of tumor growth, metastasis and host reaction”	2003

Russian Academy of Sciences, Institute of Gene Biology Moscow, Russia Lecture entitled “ <i>In vivo</i> molecular imaging with fluorescent protein”	2003
M.D. Anderson Cancer Center 1 st Course of Molecular Mechanisms in Brain Tumors Montgomery, TX Lecture entitled “Use of green fluorescent protein and red fluorescent protein to follow brain tumors and their therapy <i>in vivo</i> by whole-body imaging”	2003
National Institute of Infectious Diseases Symposia on Bioimaging and Nano-technology Tokyo, Japan Lecture entitled “Imaging analysis of angiogenesis and metastasis of cancer”	2003
Roswell Park Cancer Institute Molecular and Cellular Biophysics Department Special Seminar Buffalo, NY Lecture entitled “Multi-colored imaging of multiple events in tumor progression”	2003
76 th Annual Meeting of the Japanese Orthopaedic Association Kanazawa, Japan 1) Lecture entitled “Correlation of green fluorescent protein with standard x-ray in assessing prostate cancer bone lesions in nude mice” 2) Lecture entitled “Multicolor <i>in vivo</i> cellular and molecular imaging with GFP and RFP”	2003
15 th Annual Pezcoller Symposium (see <i>Cancer Research</i> 64 , 2929-2933, 2004) Rovereto, Italy Lecture entitled “Real-time visualization of cancer cellular and molecular biology in the intact animal”	2003
Tumor Biology Center at the University of Freiburg’s Symposium on Novel Approaches for the Discovery of Anticancer Agents. Freiburg, Germany Lecture entitled “Imaging tumor progression <i>in vivo</i> ”	2003
Dedication of Dong Fang Hospice in honor of founder Professor Jia Xi Li and in memory Of former Minister of Health Minzhang Chen Beijing, P.R. China Lecture entitled “Drug evaluation in pancreatic cancer MetaMouse”	2003
4 th International Symposium on Minimal Residual Cancer Oslo, Norway Lecture entitled “Visualizing live tumor cells interacting with host cells color-Coded with green fluorescent protein and red fluorescent protein”	2003
SPIE’s BIOS 2004 Symposium – Genetically engineered and optical probes for biomedical applications II: Genetically engineered fluorescent proteins and bioluminescent probes. San Jose, CA Lecture entitled “Dual-color imaging of tumor host interaction with GFP and RFP”	2004

26 th Annual University of California of San Diego Assembly in Surgery San Diego, CA Lecture entitled “Dual-color fluorescence imaging of tumor-host interaction with green and red fluorescent proteins”	2004
Pfizer and Howard Hughes Medical Institute Seminar Series at Connecticut College New London, CT Lecture entitled “Multi-color <i>in vivo</i> imaging: The new cell biology”	2004
95 th American Association for Cancer Research Annual Meeting – “Meet-the-Expert” Sunrise Session Orlando, FL Lecture entitled “Imaging of animal models with GFP”	2004
Kyoto University Graduate School of Medicine, Department of Pharmacology Kyoto, Japan Lecture entitled “ <i>In vivo</i> imaging with fluorescent proteins”	2004
13 th Annual Meeting of the Japanese Association for Metastasis Research Tokyo, Japan Lecture entitled “ <i>In vivo</i> imaging with fluorescent proteins”	2004
Mouse Workshop at Murinus GmbH Hamburg, Germany Lecture entitled “Multi-color fluorescence imaging <i>in vivo</i> : The new cell biology”	2004
4 th Intercontinental Meeting of the Hair Research Societies Berlin, Germany Lecture entitled “Potential of nestin-expressing hair-follicle stem cells to form neurons and blood vessels”	2004
32 nd Annual Meeting of the American Society for Photobiology Seattle, WA Lecture entitled “Multi-color <i>in vivo</i> imaging with fluorescent proteins”	2004
12 th International Congress of the Histochemistry and Cytochemistry San Diego, CA Lecture entitled “Rainbow imaging <i>in vivo</i> ”	2004
University of Washington’s Friday Harbor Laboratories Centennial Celebration - Calcium-Regulated Photoproteins and Green Fluorescent Proteins Friday Harbor, WA Lecture entitled “Imaging cell biology <i>in vivo</i> with fluorescent proteins”	2004
42 nd Annual Meeting of the Japan Society of Clinical Oncology Kyoto, Japan Lecture entitled “Multicolor imaging of tumor growth, metastasis and angiogenesis <i>in vivo</i> ”	2004

19 th Annual Meeting of the International Society for Biological Therapy of Cancer Primer on Biological Therapy of Cancer San Francisco, CA Lecture entitled "Rainbow imaging: Cell biology <i>in vivo</i> "	2004
Florescent Proteins in Drug Development <i>In Vivo</i> Molecular Imaging Cambridge Healthtech Institute La Jolla, California Lecture entitled " <i>In Vivo</i> imaging with green fluorescent proteins"	2004
19 th World Congress of International Society for Digestive Surgery Yokohama, Japan Lecture entitled: " <i>In Vivo</i> imaging with fluorescent proteins: the new cell biology"	2004
European Molecular Biology Organizations' Course on Light Microscopy Life Specimens in collaboration with the National University of Singapore, the Institute of Molecular Cell Biology, and the Institute of Bio and Nanotechnology Singapore Lecture entitled " <i>In vivo</i> imaging with fluorescent proteins: the new cell biology"	2005
SPIE's BIOS 2005 Symposium – Genetically engineered and optical probes for biomedical applications III. San Jose, CA Lecture entitled " <i>In vivo</i> imaging with fluorescent proteins: the new cell biology"	2005
Biophysical Society 49 th Annual Meeting Long Beach, CA Lecture entitled "Imaging with fluorescent proteins <i>in vivo</i> , the new cell biology"	2005
University of Texas NSF IGERT Program Seminar Austin, TX Lecture entitled " <i>In vivo</i> imaging with multi-color fluorescent proteins: The new cell biology"	2005
4 th Conference on Hyperhomocysteinemia Saarbrucken, Germany Lecture entitled "Use of methionine-homocysteine, α , γ -lyases to develop an <i>in vitro</i> Enzymatic diagnostics panel for homocysteine, cysteine, methionine and vitamin B ₆ ."	2005
Joint Congress of the Histochemical Society and the Society for Histochemistry Noordwijkerhout, The Netherlands Lecture entitled "Multi-color imaging of the multiple events of tumor progression in real-time"	2005
66 th Annual Meeting of the Society of Investigative Dermatology St. Louis, MO Lecture entitled "Nestin-positive, keratin-15-negative primitive stem cells in the hair follicle capable of forming multiple types of non-hair-follicle cells"	2005
14 th Annual Meeting of the Japanese Association for Metastasis Research Osaka, Japan Lecture entitled "Multi-color imaging of the multiple events of tumor progression in real-time"	2005

University of Texas, MD Anderson Cancer, Science Park-Research Division, Virginia Harris Cockrell Cancer Research Institute Lecture entitled "Multi-color imaging of the multiple events of tumor progression in real time"	2005
1 st International Tübingen-Symposium on Pediatric Solid Tumors Tübingen, Germany Lecture entitled "Dual-color labeling and fluorescent imaging for in vivo visualization of cytoplasmic and nuclear dynamics of cancer cell migration"	2005
63 rd Annual Meeting of the Microscopy Society of America- Microscopy and Microanalysis 2005 Honolulu, HI Lecture entitled "Multi-color in vivo imaging with fluorescent proteins: The new cell biology"	2005
10 th Anniversary Drug Discovery Technology and Development Conference Boston, MA Lecture entitled "In vivo imaging of tissues, cells, organelles, trafficking and gene expression with multicolor fluorescent proteins in real-time"	2005
Stem Cell Research: A Technology with the Promise to Contribute to All of Medicine Cambridge Healthtech Institute Lecture entitled "Hair follicle nestin-expressing stem cells can form neurons"	2005
5 th International Symposium on Minimal Residual Cancer San Francisco, CA Lecture entitled "Multi-color subcellular imaging of cancer cell dynamics in live animals"	2005
43 rd Annual Meeting of the Japan Society of Clinical Oncology Sapporo, Japan Lecture entitled "Visualizing the <i>in vivo</i> cell biology of metastasis in real time"	2005
35 th Annual European Society for Dermatological Research Tübingen, Germany Lecture entitled "Multi-potent nestin-positive keratin-negative hair-follicle bulge stem cells can form neurons"	2005
Eisai Oncology Area Committee Meeting Boston, MA Lecture entitled "Orthotopic transplantation models and GFP imaging"	2005
13 th Annual Meeting of the Society for Hair Science Research Tokyo, Japan Lecture entitled "Implanted hair follicle stem cells form Schwann cells which support repair of severed nerves and spinal cord"	2005
SPIE's BIOS 2006 Symposium – Genetically engineered and optical probes for biomedical applications. San Jose, CA Lecture entitled "Multi-color imaging with fluorescent proteins in mice"	2006

Cambridge Healthtech Institute's 13 th International Molecular Medicine Tri-Conference San Francisco, CA Lecture entitled "Orthotopic Metastatic Mouse Models: the Bridge Linking Preclinical and Clinical Development"	2006
9 th Annual Meeting of the American Society for Gene Therapy Baltimore, MD Lecture entitled "Metastatic disease in cancer"	2006
47 th Annual Meeting of the Japanese Society of Clinical Cytology Yokohama, Japan Lecture entitled "Real time multi-color subcellular imaging in mice"	2006
Genomics and Cancer 2006 – German Cancer Research Center (DKFZ) Heidelberg, Germany Lecture entitled " <i>Salmonella typhimurium</i> amino acid auxotrophs selectively target metastatic prostate and breast tumors"	2006
FEBS Advanced Course: From Functional Genomics to Molecular Proteomics Yerevan, Armenia Lecture entitled "Tri-color whole-body cellular imaging of tumor-stroma interaction and drug response in live mice"	2006
21 st Century COE Colloquium: Animal Models of Cancer Research – Kyoto University Kyoto, Japan Lecture entitled "Development of the new field of in vivo cell biology with multi-color fluorescent proteins"	2006
Dynamic Microscopy 2006 Würzburg, Germany Lecture entitled "Whole-body subcellular imaging in the live animals"	2006
18 th Annual Meeting of the Korean Society for Molecular and Cellular Biology Seoul, Korea Lecture entitled "Subcellular imaging in living mice: The new cell biology"	2006
2006 Hwasun Optical Imaging Workshop & Symposium Seoul, Korea Lecture entitled "Targeted therapy with a <i>Salmonella typhimurium</i> Leucine-Arginine auxotroph cures orthotopic human breast tumors in nude mice"	2006
14 th Symposium on Bioluminescence and Chemiluminescence San Diego, CA Lecture entitled "Subcellular imaging in vivo: The new cell biology"	2006
Cambridge Healthtech Institute's 3 rd Annual Fluorescent Proteins in Drug Development La Jolla, California Lecture entitled "Whole-body subcellular imaging in the live mouse"	2006
International Symposia for Bioimaging Kyoto, Japan Lecture entitled "Subcellular imaging in vivo: The new cell biology"	2006

- Joint Meeting of the 3rd ISC International Conference on Cancer Therapeutics and the 11th International Symposium on Cancer Chemotherapy 2006
Tokyo, Japan
Lecture entitled “The use of fluorescent proteins imaging to visualize new cellular and subcellular targets for cancer chemotherapy *in vivo*”
- SPIE’s BIOS 2007 Symposium – Genetically engineered and optical probes 2007
for biomedical applications.
San Jose, CA
Lecture entitled “Tri-color whole-body cellular imaging of tumor-stroma interaction and drug response in live mice”
- Keystone Symposium on Imaging Immune Response 2007
Keystone, CO
Lecture entitled “Tri-color imaging of interaction of the host immune system and tumor Cells in the living mouse”
- 79th Japanese Gastric Cancer Meeting 2007
Nagoya, Japan
Lecture entitled “The use of fluorescent protein imaging to visualize new cellular and subcellular targets for cancer chemotherapy *in vivo*”
- 3rd International Conference on Stem Cell Research and Therapeutics 2007
San Diego, CA
Lecture entitled “Multipotency of Hair Follicle Stem Cells to Form Neural Cells
- 143rd Meeting of the Japanese Society of Veterinary Medicine 2007
Tsukuba City, Japan
Lecture entitled “Subcellular imaging *in vivo*: The new cell biology”
- Annual Meeting of the American Society for Investigative Pathology at 2007
Experimental Biology 2007
Washington, DC
Lecture entitled “Whole-body subcellular multicolor imaging of tumor-host interaction and drug response in real time”
- 54th Annual Meeting of the Japanese Meeting of Animal Science 2007
Tokyo, Japan
Lecture entitled “Whole-body subcellular multicolor imaging of tumor-host interaction and drug response in real time”

Most Cited Publications of Robert M. Hoffman

1. Hoffman, R.M. Altered methionine metabolism, DNA methylation and oncogene expression in carcinogenesis. A review and synthesis. *Biochim. Biophys. Acta* **738**, 49-87, 1984. (No. of citations: 275)
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13. Hoffman, R. Green fluorescent protein imaging of tumour growth, metastasis, and angiogenesis in mouse models. *Lancet Oncology* **3**, 546-556, 2002. (No. of citations: 92)

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